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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/087,082	02/28/2002	Wolfgang Dietmaier	18668-US1	3192

22829 7590 05/17/2005

ROCHE MOLECULAR SYSTEMS INC
PATENT LAW DEPARTMENT
1145 ATLANTIC AVENUE
ALAMEDA, CA 94501

EXAMINER	
CHUNDURU, SURYAPRABHA	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 05/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/087,082	DIETMAIER ET AL.	
	Examiner	Art Unit	
	Suryaprabha Chunduru	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 February 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

S.O.O.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 23, 2005 has been entered.

Status of the Application

2. The action is in response to the RCE filed on April 23, 2005. Currently claims 1, 3-17 are pending. Claim 2 is cancelled. All arguments and amendment have been fully considered and thoroughly reviewed and deemed persuasive in view of the amendment.

Priority

3. This instant application filed on 2/28/2002 is a continuation of US non-provisional 09/270,933 filed on March 16/1999 now PAT 6,365,375. and claims foreign priority to Germany 198 13 317.0 filed on 3/26/1998. Receipt is acknowledged of papers (certified copies filed on 3/22/2004) submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file. Perfecting a claim to priority under 35 U.S.C. 119(a)-(d) within the time period set in 37 CFR 1.55(a)(1) or filing a grantable petition under 37 CFR 1.55(c). See MPEP § 201.13. The foreign priority filing date must antedate the reference and be perfected. The filing date of the priority document is not perfected unless applicant has filed a certified priority document in the application (and an English language translation, if the document is not in English) (see 37

CFR 1.55(a)(3)). For the examination purposes the effective filling date March 16, 1999 is considered as the earliest priority date.

Specification

4. It is noted that in brief description of figures on page of the specification, Fig. 8 recites upper gel and lower gel, however, the Fig.8 shows two parts as A and B. This is only an observation but not an objection to the specification. For the clarity purposes upper gel and lower gel can be described as A and B.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Note: Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Claims 1, 3, 5-11, 13-17 are rejected under 35 U.S.C. 102(a) as being anticipated by Dietmaier et al. (American Journal of Pathology, Vol. 154, No.1, page 83-95, January 1999).

Dietmaier et al. teach a method of claims 1 and 9, for the amplification of nucleic acid fragments from a sample, wherein said nucleic acid fragments are between 100 and 1000 base pairs in length (see page 89, Fig. 2, indicating the nucleic acid fragments of 200 bp to 230 base pairs), said method comprising first (pre amplification primer extension) and second (specific

amplification) thermocyclic amplification reactions, wherein said first amplification is carried out using completely randomized primers (see page 85, col. 1, paragraphs 1-2 under whole genome amplification by PEP-PCR, I-PEP-PCR and DOP-PCR section), said second amplification reaction is carried out using specific primers (see page 85, col. 2, paragraph 1 under single-round multicycle PCR after I-PEP and paragraph 1 under detection of p53 mutations after preamplification by I-PEP sections), and said first and second amplification reactions are carried out using the same mixture of at least two DNA polymerases, atleast one of which possesses 3'5'exonulcease (fidelity or proofreading activity) (see page 85, col. 1, paragraphs 1-2 under whole genome amplification by PEP-PCR, I-PEP-PCR and DOP-PCR section, col. 2, paragraph 1 under single-round multicycle PCR after I-PEP and paragraph 1 under detection of p53 mutations after preamplification by I-PEP sections, indicating use of two polymerases (Taq DNA polymerase and Pwo polymerase (high fidelity polymerase) or Expand high fidelity polymerase), in both first and second amplification reactions).

With regard to claim 3, 5, 10-11, 13, 17, Dietmaier et al. teach that said mixture of DNA polymerases comprises at least two thermostable polymerases, wherein the mixture comprises a DNA polymerase without 3'-5' exonuclease, (Taq DNA polymerase) and a DNA polymerase with 3'-5' exonuclease activity (Pwo DNA polymerase) (see page 85, col. 1, line 3 of paragraph 2 under whole genome amplification by PEP-PCR, I-PEP-PCR and DOP-PCR section, and col. 2, line 1-2);

With regard to claims 6, 14, Dietmaier et al. teach that said sample comprises cells (see page 84, col. 2, paragraphs 1-3 under Materials and methods section);

With regard to claims 7-8, 15-16, Dietmaier et al. teach that said method further comprises treating said sample of cells with protenase prior to the thermocylcic reactions and said protease is proteinase K (see page 84, col. 2, paragraph 2 under materials and methods section);

With regard to claim 9, Dietmaier et al. teach that in said first amplification reaction, the temperature at which primer extension is carried out is increased at least some of the successive amplification cycles (see page 85, col. 2, line 3-13). Accordingly the instant claims are anticipated by Dietmaier et al.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Eggeling et al. (Hum Genet., Vol. 99, pages 266-270, 1997) in view of Biochemicals Catalog, (Biochemicals Catalog, Boehringer Mannheim, page 153, 1997).

Eggeling et al. teach a method of claims 1, 9, for the amplification of nucleic acid fragments from a sample, wherein said nucleic acid fragments are between 100 and 1000 base pairs (see page 267, col. 2, line 4-7 under Results section) said method comprises first (primer extension pre amplification) and second (specific amplification), wherein said first amplification is carried out using completely randomized primers (see page 267, column 1, paragraph 3 of materials and methods section) and said second amplification reaction is carried out using specific primers (see page 267, column 1, paragraph 5 under Materials and methods section) and wherein in said first amplification reaction, the temperature at which primer extension is carried out is increases in at least some of the successive amplification cycles (see page 267, col. 1, paragraph 3, of materials and methods section).

With regard to claims 6, 14, Eggeling et al. teach that said sample comprises cells (blood cells) (see page 267, column 1, paragraph 1 under materials and methods);

With regard to claims 7-8, 15-16, Eggeling et al. treating sample of cells with proteinase K (see page 267, column 1, paragraph 2 under materials and methods section);

However, Eggeling et al. did not teach use of a mixture of at least two thermostable DNA polymerases, said mixture comprising at least one DNA polymerase without 3'-5' exonuclease activity and a DNA polymerase with 3'-5' exonuclease activity and said sample comprising a pool of cDNAs.

With regard to claims 1, 3-17, Biochemicals Catalog teaches use of a mixture of at least two thermostable DNA polymerases (Expand™ high fidelity polymerases) for amplification of nucleic acid fragments up to 6 kb which includes nucleic acid fragments between 1 base and 6kb in length) (see page 153, col. 1, line 10-16 of paragraph 2, col. 2, Fig. Indicating various PCR fragments ranging from 145 bp to 4kb in length) and said mixture of DNA polymerases comprises a DNA polymerase without 3'-5' exonuclease activity (Taq DNA polymerase) and a DNA polymerase with 3'-5' exonuclease activity (Pwo DNA polymerase) (see page 153, col. 1, line 5-8, of paragraph 1, line 10-16 of paragraph 2, as claimed in claims 5, and 13).

With regard to claims 4, 12, Biochemical Catalog teaches amplification of cDNA population using said mixture of DNA polymerases (see page 153, col. 1, line 4-9 of paragraph 3).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to amplify nucleic acid fragments of Eggeling et al. in a manner taught by Biochemicals Catalog using the mixture of DNA polymerases (Expand™ high fidelity polymerases) having high fidelity to achieve expected benefit of developing an enhanced sensitive method of amplification because Biochemicals Catalog taught that the use of the combination of DNA polymerases reduces secondary structures and provides lower error rate and provides high fidelity PCR system in amplifying entire population of transcripts without the need to construct cDNA libraries (see page 153, col. 1, line 10-16 of paragraph 2, line 4-9 of paragraph 3). An ordinary practitioner would have been motivated to combine the method of amplification of a nucleic acid as taught by Eggeling et al. with the step of adding a mixture of at least two DNA polymerases in order to achieve low error rate during primer extension. The

ordinary artisan would have a reasonable expectation of success that inclusion of the mixture of DNA polymerases would result in an increase in fidelity as compared to the use of a single DNA polymerase and such modification of the method would be obvious over the cited prior art in the absence of secondary considerations.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 571-272-0783. The examiner can normally be reached on 8.30A.M. - 4.30P.M , Mon - Friday,.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Prabha Chunduru 5/16/05
Suryaprabha Chunduru
Examiner
Art Unit 1637